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			U.S. PATENT			
Examiner	Cite	Document Number	Publication Date	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant	
Initials * No	No.1	Number - Kind Code ² (# known)	MM-DD-YYYY	Gled Dodnien	Passages or Relevant Figures Appear	
/AB/	AA	US-5,721,138	02-24-1998	Lawn		
1	AB	US-5,866,551	02-02-1999	Benoit et al.		
	AC	US-5,801,154	09-01-1998	Baracchini et al.	•	
	AD	US-6,008,344	12-28-1999	Bennett et al.		
	AE US-6,080,580		06-27-2000 Baker et al.			
	AF	US-6,512,161	01-28-2003 Rouy et al.			
	ÅG	US-6,573,050	06-03-2003	Ben-David et al.		
1	AH	US-6,613,567	09-02-2003	Bennett et al.		
1	Αĭ	US-6,809,193	10-26-2004	McKay et al.		
77	AJ	US-2003/0119766	06-26-2003	Crooke et al.		
	AK	US-2004/0242516	12-02-2004	Crooke et al.		
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Fuendese	Cito	Foreign Patent Document	Document Publication	Name of Patentes or	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	
Examiner Initials*	_/v/_1_4	Country Code ³ - Number ⁴ - Kind Code ⁶ (<i>if Imown</i>)	Date MM-DD-YYYY	Applicant of Cited Document		τ°
/AB/	AL	WO 96/09392 A1	03-28-1996	Ribozyme Pharm.		
- 1	AM	WO 99/34016 A2	07-08-1999	Genena Ltd.		
	AN	WO 99/35241 A1	07-15-1999	Rhone-Poulenc		
7/	AO	WO 03/014307 A2	02-20-2003	Isis Pharma.		
_ V	AP	WO 2005/000201 A2	01-06-2005	Isis Pharma.		

Examiner Signature	/Amy Bowman/	Date Considered	05/08/2007

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		NON PATENT LITERATURE DOCUMENTS			
Examiner Cite No.1					
/AB/ AQ		AGRAWAL, S., "Antisense oligonucleotides: towards clinical trials," <i>TIBTECH</i> (1996) 14:376-387.			
	AR	ANDERSON, L. et al., "A comparison of selected mRNA and protein abundances in human liver," <i>Electrophoresis</i> (1997) 18:533-537.			
AS		BRAASCH, D. A. et al., "Novel Antisense and Peptide Nucleic Acid Strategies for Controlling Gene Expression," <i>Biochem.</i> (2002) 41(14):4503-4510.			
	AT	BRANCH, A. D., "A good antisense molecule is hard to find," TIBS (1998) 23:45-50.			
	AU	CALLOW, M. J. et al., "Expression of human apolipoprotein B and assembly of lipoprotein (a) in transgenic mice," <i>Proc. Natl. Acad. Sci. USA</i> (1994) 91:2130-2134.			
AV Lipoprotein into Transgenic Mice Expressing Human Apolipoprotein (a)," J. Biol. Ch		CHIESA, G. et al., "Reconstitution of Lipoprotein (a) by Infusion of Human Low Density Lipoprotein into Transgenic Mice Expressing Human Apolipoprotein (a)," J. Biol. Chem. (1992) 267(34):24369-24374.			
	AW	CHIN, A., "On Preparation and Utilization of Isolated and Purified Oligonucleotides," Katherine R. Everett Law Library of the University of North Carolina, March 14, 2002.			
	AX	DEVERRE, JR. et al., "A competitive enzyme hybridization assay for plasma determination of phosphodiester and phosphorothioate antisense oligonucleotides," <i>Nucleic Acids Res.</i> (1997) 25(18):3584-3589.			
	AY	DIAS, N. et al., "Potential roles of antisense oligonucleotides in cancer therapy. The example of bcl-2 antisense oligonucleotides." Eur. J. Pharm. Biopharm. (2002) 54:263-269.			
	AZ	FRANK, S. et al., "Advenovirus-mediated apo(a)-antisense-RNA expression efficiently inhibits apo(a) synthesis in vitro and in vivo," <i>Gene Therapy</i> (2001) 8:425-430.			
BA FRANK, S. et al., "The apolipoprotein(a) gene resides on human chromosome 6q26-27, in close proximity to the homologous gene for plasminogen," Hum. Genet. (1988) 79(4):352-356.					
	ВВ	FRITZ, H. et al., "Cationic Polystyrene Nanoparticles: Preparation and Characterization of a Model Drug Carrier System for Antisense Oligonucleotides," J. Colloid Interface Sci. (1997) 195:272-288.			
\overline{V}	ВС	GEWIRTZ, A. M. et al., "Facilitating oligonucleotide delivery: Helping antisense deliver on its promise," <i>Proc. Natl. Acad. Sci. USA</i> (1996) 93:3161-3163.			

Examiner	/Amy Rowman/	Date	05/08/2007
Signature	/Amy Bowman/	Considered	00,00,2001

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INCORMATION DIGGLOCURE	Application Number	10/559,647
INFORMATION DISCLOSURE	Filing Date	07/31/2006
STATEMENT BY APPLICANT	First Named Inventor	Rosanne M. Crooke
	Art Unit	1635
(Use as many sheets as necessary)	Examiner Name	Amy Hudson Bowman
Sheet 3 of 4	Attorney Docket Number	ISPH-0595USA

		NON PATENT LITERATURE DOCUMENTS			
Examiner Cite No.1					
/AB/ _{BD}		GRAINGER, D. J. et al., "Activation of transforming growth factor-β is inhibited in transgenic apolipoprotein(a) mice," <i>Nature</i> (1994) 370:460-462.			
	BE	GREEN, D. W. et al., "Antisense Oligonucleotides: An Evolving Technology for the Modulation of Gene Expression in Human Disease," J. Am. Coll. Surg. (2000) 191:93-105.			
	BF	HAJJAR, K. A. et al., "The Role of Lipoprotein(a) in Atherogenesis and Thrombosis," Annu. Rev. Med. (1996) 47:423-442.			
	BG	JEN, KY. et al., "Suppression of Gene Expression by Targeted Disruption of Messenger RNA: Available Options and Current Strategies," Stem Cells (2000) 18:307-319.			
	ВН	KATAN, M. B. et al., "Characteristics of Human Hypo- and Hyperresponders to Dietary Cholesterol," Am. J. Epidemiology (1987) 125(3):387-399.			
	BI	KOSTNER, K. M. et al., "Lipoprotein(a): still an enigma?" Current Opinion in Lipidology (2002) 13:391-396.			
	ВЈ	LAWN, R. M. et al., "Atherogenesis in transgenic mice expressing human apolipoprotein(a)," Nature (1992) 360:670-672.			
	ВК	MCLEAN, J. W. et al., "cDNA sequence of human apolipoprotein(a) is homologous to plasminogen," <i>Nature</i> (1987) 330:132-137.			
	BL	MILLIGAN, J. F. et al., "Current Concepts in Antisense Drug Design," J. Med. Chem. (1993) 36(14):1923-1927.			
	вм	MORISHITA, R. et al., "Novel Therapeutic Strategy for Atherosclerosis – Ribozyme Oligonucleotides Against Apolipoprotein(a) Selectively Inhibit Apolipoprotein(a) But Not Plasminogen Gene Expression," Circulation (1998) 98:1898-1904.			
	BN	NOWAK-GŌTTL, U. et al., "Lipoprotein (a): Its Role in Childhood Thromboembolism," Pediatrics (1997) 99(6):1-3.			
	во	OHMICHI, T. et al., "The virtues of self-binding: high sequence specificity for RNA cleavage by self-processed hammerhead ribozymes," <i>Nucleic Acids Res.</i> (2000) 28(3):776-783.			
V	BP	OPALINSKA, J. B. et al., "Nucleic-Acid Therapeutics: Basic Principles and Recent Applications," Nature Reviews Drug Discovery (2002) 1:503-514.			

Examiner	/Amy Bowman/	Date	05/08/2007
Signature	/Ally Downlan	Considered	03/00/200/

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Subst	itute for form 144	19/PTO		Complete if Known		
	COBLAT	ION DIO	OL OCUDE	Application Number	10/559,647	
			CLOSURE	Filing Date	07/31/2006	
ST	ATEMEN	IT BY A	PPLICANT	First Named Inventor	Rosanne M. Crooke	
				Art Unit	1635	
•	(Use as m	any sheets as	necessary)	Examiner Name	Amy Hudson Bowman	
Shee	nt 4	of	4	Attorney Docket Number	ISPH-0595USA	

	NON PATENT LITERATURE DOCUMENTS		
BQ	PROSNYAK, M. I. et al., "Substitution of 2-Aminoadenine and 5-Methylcytosine for Adenine and Cytosine in Hybridization Probes Increases the Sensitivity of DNA Fingerprinting," Genomics (1994) 21:490-494.		
BR	RAINWATER, D. L. et al., "Lipoprotein Lp(a): Effects of Allelic Variation at the LPA Locus," J. Exp. Zoology (1998) 282:54-61.		
BS	SANDKAMP, M. et al., "Lipoprotein(a) is an Independent Risk Factor for Myocardial Infarction at a Young Age," Clin. Chem. (1990) 36(1):20-23.		
вт	SEED, M. et al., "Relation of Scrum Lipoprotein(a) Concentration and Apolipoprotein(a) Phenotype to Coronary Heart Disease in Patients with Familial Hypercholesterolemia," New Engl. J. Med. (1990) 322:1494-1499.		
BU	SKERRA, A., "Phosphorothioate primers improve the amplification of DNA sequences by DNA polymerase with proofreading activity," <i>Nucleic Acids Res.</i> (1992) 20(14):3551-3554.		
BV	TAMM, I. et al., "Antisense therapy in oncology: new hope for an old idea?" The Lancet (2001) 358:489-497.		
BW	VESSBY, B. et al., "Diverging Effects of Cholestyramine on Apolipoprotein B and Lipoprotein Lp(a)," Atherosclerosis (1982) 44:61-71.		
вх	WEINTRAUB, H. M., "Antisense RNA and DNA," Scientific American (1990) 40-46.		
вч	YANG, Y. et al., "Transforming Growth Factor-β1 Inhibits Human Keratinocyte Proliferation by Upregulation of a rEceptor-Type Tyrosine Phosphatase R-PTP-κ Gene Expression," Biochem. Biophys. Res. Commun. (1996) 228:807-812.		
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	BQ BR BS BT BU BV BW BX	Cite No. Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the ltem (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published. PROSNYAK, M. I. et al., "Substitution of 2-Aminoadenine and 5-Methylcytosine for Adenine and Cytosine in Hybridization Probes Increases the Sensitivity of DNA Fingerprinting," <i>Genomics</i> (1994) 21:490-494. BR RAINWATER, D. L. et al., "Lipoprotein Lp(a): Effects of Allelic Variation at the <i>LPA</i> Locus," <i>J. Exp. Zoology</i> (1998) 282:54-61. BS SANDKAMP, M. et al., "Lipoprotein(a) is an Independent Risk Factor for Myocardial Infarction at a Young Age," <i>Clin. Chem.</i> (1990) 36(1):20-23. BT SEED, M. et al., "Relation of Scrum Lipoprotein(a) Concentration and Apolipoprotein(a) Phenotype to Coronary Heart Disease in Patients with Familial Hypercholesterolemia," <i>New Engl. J. Med.</i> (1990) 322:1494-1499. BU SKERRA, A., "Phosphorothioate primers improve the amplification of DNA sequences by DNA polymerase with proofreading activity," <i>Nucleic Acids Res.</i> (1992) 20(14):3551-3554. BV TAMM, I. et al., "Antisense therapy in oncology: new hope for an old idea?" <i>The Lancet</i> (2001) 358:489-497. BW VESSBY, B. et al., "Diverging Effects of Cholestyramine on Apolipoprotein B and Lipoprotein Lp(a)," <i>Atherosclerosis</i> (1982) 44:61-71. BX WEINTRAUB, H. M., "Antisense RNA and DNA," <i>Scientific American</i> (1990) 40-46.	

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